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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/869,677	10/09/2001	Lars Bjorck	100084.416USPC	8541

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EXAMINER	
GRASER, JENNIFER E	
ART UNIT	PAPER NUMBER
1645	17

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/869,677	Applicant(s) Bjorck et al.
	Examiner Jennifer Graser	Art Unit 1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *Election, 5/7/03*

2a)☐ This action is **FINAL.** 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above, claim(s) *4-9* is/are withdrawn from consideratio

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 10-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☒ All b)☐ Some* c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15)☒ Notice of References Cited (PTO-892)

16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 9

18)☐ Interview Summary (PTO-413) Paper No(s). _____

19)☐ Notice of Informal Patent Application (PTO-152)

20)☐ Other:

DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Group I, claims 1-3 and 10-12, in Paper No. 16 is acknowledged. The traversal is on the ground(s) that the search of the entire application would not place a serious burden on the Examiner. This has been fully considered is not found persuasive because the three Groups all possess different special technical features and therefore do not relate to a single general inventive concept. The three special technical features, DNA, proteins and antibodies, are biologically, structurally and chemically different products and therefore they are patentably distinct and independent inventions. The search for the protein will not necessarily reveal art for the DNA or the antibody. The literature search for the 3 inventions is not coextensive. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

The requirement is still deemed proper and is therefore made **FINAL**. Claims 4-9 are withdrawn from examination because they are drawn to a non-elected invention.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-3 and 10-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 2 are confusing and unclear because they recite a polypeptide which comprises the amino acid sequence of SEQ ID NO:1; however, SEQ ID NO:1 is a nucleic acid sequence. The Electronic Sequence Listing filed by Applicants reveals that it is SEQ ID NO:**2** which sets forth the amino acid sequence. Applicants must amend the claims to recite the proper sequence identifier, i.e., "the amino acid sequence of SEQ ID NO:2".

Claims 1 and 2 are also vague and indefinite because the claims do not recite that the polypeptide is isolated or purified. Accordingly, it is unclear if the polypeptide is on the surface of a bacterium, i.e., a product of nature. The claims must be amended to recite that the polypeptide is 'isolated and purified' or a rejection under 35 USC 101 will be made.

Claims 1 and 2 are vague and indefinite because it is unclear what is encompassed by the term "variant". Is this a completely different protein? It is noted that part (c) of claims 1 and 2 reads on fragments of variants. This language encompasses polypeptides which have not been disclosed in the specification, i.e, a fragment of a variant could include the amino acids which vary from the protein of SEQ ID NO:2. See 112, 1st enablement rejection below.

Claim 1, part (b) is vague and indefinite because it is unclear what is represented by "an anti-MtsA antibody". First, it is unclear if the use of the term "anti" is implying that the antibody is an anti-idiotypic antibody and, second, it is unclear what the term "MtsA" represents. The

name "MtsA" is not sufficient to identify the antibody. The claim should provide any structural properties, such as the amino acid sequence of the antibody, which would allow for one to identify the recited antibody, and hence the fragment which is being claimed, without ambiguity. The mere recitation of a name does not adequately define the antibody to which the fragment binds. While the specification can be used to provide definitive support, the claims are not read in a vacuum. Rather, the claim must be definite and complete in and of itself. Limitations from the specification will not be read into the claims. The claims as they stand are incomplete and fail to provide adequate structural properties to allow for one to identify what is being claimed. It appears that Applicants intend to claim "and an immunogenic fragment thereof which specifically binds to a polypeptide having the amino acid sequence forth in SEQ ID NO:2".Clarification is requested.

Claim 1, parts (b) and (c) and claim 2, parts (b) and (c) are vague and indefinite due to the term "capable of". Having the capability is not the same thing as actually performing the function. A positive recitation of the function is required. Suggested language is "which specifically binds".

Claim 12 provides for the "use" of the polypeptide, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced. Claim 12 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the

process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-3 and 10-12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The breadth of the instant claims contains proteins and peptides other than what is specified in the sequence disclosure. The specification states that substitutions, additions, or deletions may be made to the defined sequences, i.e., "variants"; however, the specification provides no guidance as to what amino acids may be changed without causing a detrimental effect to the protein to be produced. Further, it is unpredictable as to which amino acids could be removed and which could be added. While it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where amino acid substitutions can be made with a reasonable expectation of success are limited. Other positions

are critical to the protein's structure/function relationship, e.g., such as various positions or regions directly involved in binding, catalysis in providing the correct three-dimensional spacial orientation of binding and catalytic sites. These regions can tolerate only very little or no substitutions. Selective point mutation to one key antigen residue eliminate the ability of an antibody to recognize this altered antigen. If the range of decreased binding ability after single point mutation of a protein antigen varies, one could expect point mutations in the protein antigen to cause varying degrees of loss of protection, depending on the relative importance to the binding interaction of the altered residue. Alternatively, the combined effects of multiple changes in an antigenic determinant could again result in loss of protection. A protein having multiple antigenic sites, multiple point mutations, or accumulated point mutations at key residues could create a new antigen that is precipitously or progressively unrecognizable by any of the antibodies in the polyclonal pool. Thus, proteins of different levels of homology may not induce antibody which is recognized by the "native" protein of the *Streptococcus* bacteria, and be ineffective in a vaccine composition against *Streptococcus*.

Applicants have not shown that the full-length protein as set forth in SEQ ID NO:2 is effective as a vaccine. The specification does not provide any examples which demonstrate that the protein can generate an immunoprotective response. While the specification has shown that the protein is immunogenic and can induce antibodies in mice, it does not demonstrate that these antibodies can protect against *Streptococcus*. Im order to enable a "vaccine" or a "method of vaccinating" against a disease caused by a bacterium such as *Streptococcus*, challenge

experiments have to be shown. The bacterial vaccine art is highly unpredictable and often times a protein is capable of generating antibodies, yet is then shown to be ineffective in protecting against disease. However, methods of "treating" do not require as stringent a test.

The specification also has not identified any specific fragments or variants which could protect against disease caused by a *Streptococcus* strain (claim 3). The location of "protective" epitopes has not been provided. Often it takes more than one epitope to provide protection. Accordingly, claims to synthetic protective epitope(s) , fragments and variants are not enabled. Additionally, there is no correlation that a fragment, peptide or variant which binds a protein having the amino acid sequence of SEQ ID NO:2 would be protective.

Applicants have provide no guidance to enable one of ordinary skill in the art how to determine, without undue experimentation, the effects of different amino acid substitutions and the nature and extent of the changes that can be made, nor have they identified specification location of epitopes which are protective. Given the lack of guidance contained in the specification and the unpredictability for determining acceptable amino acid substitutions, one of skill in the art could not make or use the broadly claimed invention without undue experimentation.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

7. Claims 1-3 and 10-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Russel et al (US 5,422,427) or its equivalent (WO 93/10238).

Russel et al teach a protein fragment from Streptococcus which is identical to fragment 181-208 of Applicants' SEQ ID NO:2, i.e. 28 amino acids in length. This fragment is "at least 6 amino acids in length" and would inherently be capable of binding an anti-MtsA antibody. Column 3, lines 50-60, specifically teach fragments of least 5 contiguous amino acids in length. Column 5, lines 23-35 teach that the polypeptide or fragments may be used in vaccines to protect against pneumococcal disease. The *Streptococcus* the polypeptide is isolated from is a group A *Streptococcus*. See attached sequence alignment.

8. Claims 1-3 and 10-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Sampson et al (US 5,854,416).

Sampson et al teach an isolated polypeptide from *S.pneumoniae* which is 80% identical to Applicants' SEQ ID NO:2. The protein is therefore considered a variant of SEQ ID NO:2. The references teaches that fragments of this protein can be used as vaccines. It is taught that the fragments can be at least 10 amino acids in length. There are several fragments of this protein which are identical to the 6 amino acid length fragments of Applicants' SEQ ID NO:2. These

identical fragments would have the capability of binding to an anti-MtsA antibody. See attached sequence alignment.

9. Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Ganeshkumar et al (Infect. Immun. 1991. 59: 1093-1099)

Ganeshkumar et al teach a protein fragment from a Streptococcus saliva-binding protein which is identical to fragment 111-130 of Applicants' SEQ ID NO:2, i.e. 20 amino acids in length. This fragment is "at least 6 amino acids in length" and would inherently be capable of binding an anti-MtsA antibody. See attached sequence alignment.

Status of Claims:

10. No claims are allowed. It is noted that 'an isolated polypeptide comprising the amino acid sequence set forth in SEQ ID NO:2' is free of the prior art. However, the prior art has revealed numerous proteins which have a high degree of similarity to the protein having SEQ ID NO:2. In addition, most of these references teach fragments derived from these similar proteins. Therefore, it is suggested that perhaps Applicants' claim a larger contiguous size limitation depending on the specific support in the specification in order to include the scope of fragments in their patent coverage, i.e., an isolated polypeptide comprising at least 50 (100, etc.) contiguous amino acids of SEQ ID NO:2. However, vaccines or methods of vaccinating using these fragments is not enabled by the instant specification. See 112, first rejection above. Additional evidences must be provided in order to obtain the scope which covers this protection, i.e, results

from challenge experiments. It is noted that 'immunogenic compositions' or 'pharmaceutical compositions' and 'methods of treating' do not require as much evidence.

11. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15,1989). The Group 1645 Fax number is (703) 308-4242 which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer E. Graser whose telephone number is (703) 308-1742. The examiner can normally be reached on Monday-Friday from 7:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

J Graser 5/22/03

JENNIFER E. GRASER
PRIMARY EXAMINER